

## REMARKS

Claims 1-16, 18-27 and 32-43 are in this application. Claims 16, 18 and 39-42 were examined. Claims 1-15, 19, 20, 22, 23, 25-27 and 32-38 are withdrawn.

According to page 3 of the Office Action, claims 16, 18 and 39-42 are rejected, as being obvious over Liu et al. (Biochem. Cell Biol., Vol. 78, 2000, 447-453) and Barone et al. (US patent 5,405,863). This is respectfully traversed.

According to page 3 of the Office Action, the Examiner has accepted that although Liu et al. teach that pineal indoles such as 5-methoxytryptamine have antioxidative properties and are potent scavengers of free radicals, Liu et al. fails to disclose that such pineal indoles such as 5-methoxytryptamine can be used to treat cardiac toxicity, myocardial ischemia, myocardial infarction or heart failure.

On the same page of the Office Action, the Examiner states that Barone et al. teach that antioxidants or oxygen radical scavengers can protect the cardiovascular system including the heart from oxidative damage, particularly myocardial infarction. The Examiner also states that the antioxidant enzymes such as superoxide dismutase are taught to treat the significant increase in lipid peroxidation in patients with myocardial infarction.

The applicants found surprisingly, that 5-methoxytryptamine can lower the elevated CK-MB levels and hence could be used as an efficient cardioprotective agent. Measurement and lowering of CK-MB levels is the "Gold Standard."

Applicants bring to the Examiner's attention that none of the antioxidants or oxygen radical scavengers except 5-methoxytryptamine possesses the quality of lowering the elevated CK-MB. For Example melatonin (an analog of 5-methoxy tryptamine), which is also an antioxidants or oxygen radical scavenger, but melatonin fails to lower down the elevated level of CK-MB. Applicants remind the Examiner that

comparative data was included in the last response and this data showed that melatonin, an analog, does not show any reducing effect in CK-MB level.

The applicants are not aware of nor has the Examiner cited literature, wherein the effect of melatonin on circulating levels of CK-MB was observed. As stated above, CK-MB is the gold standard for assessing myocardial damage.

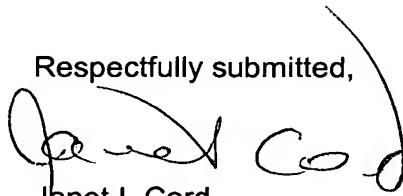
Considering the teachings of both references together, it is clear that the claimed invention is nonobvious. The first column on page 448 of Liu teaches that melatonin, 5-methoxytryptamine and 5-methoxytryptophol have different effects on different enzymes in different organs under different conditions. As the Examiner noted and as discussed above, this reference does not disclose nor suggest that the antioxidants or free radical scavengers can be used to treat cardiac toxicity. Furthermore, in column 1, lines 3-5 and in column 3, reference is made to injury associated myocardial infarction. There is neither suggestion nor disclosure in Barone that "certain" hydroxycarbazole compounds would have any effect on cardiac conditions that result from the administration of an anthracycline antineoplastic drug. Given this and the disclosure of Liu that activity and effect is organ and condition specific, there is no suggestion nor disclosure in the combination of references that 5-Methoxy tryptamine or a pharmaceutically acceptable salt thereof can be used to treat cardiac toxicity, myocardial ischemia, myocardial infarction or heart failure wherein the cardiac toxicity, myocardial ischemia, myocardial infarction or heart failure is induced by an anthracycline antineoplastic.

Therefore, in view of the discussion above concerning the scope and content of the prior art of Liu et al. and Barone et al.; the differences between the prior art and the claims at issue the level of ordinary skill in the pertinent art and the fact that that references considered as a whole do not suggest the desirability and thus the obviousness of making the combination; it is clear that claims 16, 18, and 39-43 are patentable.

Therefore, it is respectfully requested that the rejection be withdrawn.

It is submitted that the present application is in condition for allowance and favorable consideration is respectfully

Respectfully submitted,



Janet I. Cord  
Ladas & Parry LLP  
26 W. 61<sup>st</sup> Street  
New York, NY 10026  
Reg. No. 33,778  
Tel. No.: (212)708-1935